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14. ABSTRACT Over the course of the last year, the study team received IRB approval and began recruiting participants from the remaining study site, Ft. Bragg, and continued recruitment at the other five study sites (Joint Base Lewis-McChord, Ft. Bliss, Ft. Campbell, Ft. Carson, and Ft. Stewart). As of August 31, 2013, 1,320 total referrals across the six sites had been received; 666 participants had been enrolled and randomized into the study (332 participants into the STEPS UP arm; 334 participants into the optimized usual care arm); 556 participants completed the 3-month follow-up assessment; 418 participants completed the 6-month follow-up; and 181 participants completed the 12-month follow-up. At the end of June 2013 we stopped recruitment at five sites (JBLM, Ft. Bliss, Ft. Carson, Ft. Stewart, and Ft. Bragg), and stopped recruitment at Ft. Campbell at the end of July 2013. Multiple amendments have been approved by the WRNMMC IRB, including allowing for reimbursement for trial participation and offering multiple methods for collecting follow-up data. The study intervention has been refined; we continue site personnel training and coaching in the intervention and study procedures as well.					
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INTRODUCTION:

The purpose of the STEPS UP (STepped Enhancement of PTSD Services Using Primary Care) trial is to compare centralized telephonic care management with preference-based stepped PTSD and depression care to optimized usual care. We hypothesize that the STEPS UP intervention will lead to improvements in (1) PTSD and depression symptom severity (primary hypothesis); (2) anxiety and somatic symptom severity, alcohol use, mental health functioning, work functioning; (3) costs and cost-effectiveness. We further hypothesize that qualitative data will show (4) patients, their family members, and participating clinicians find that the STEPS UP intervention is an acceptable, effective, and satisfying approach to deliver and receive PTSD and depression care

STEPS UP is a six-site, two-parallel arm (N = 1,500) randomized controlled effectiveness trial with 3-month, 6-month, and 12-month follow-up comparing centralized telephonic stepped-care management to optimized usual PTSD and depression care. In addition to the existing PTSD and depression treatment options, STEPS UP will include web-based cognitive behavioral self-management, telephone cognitive-behavioral therapy, continuous RN nurse care management, and computer-automated care management support. Both arms can refer patients for mental health specialty care as needed, preferred and available. The study uses sites currently running RESPECT-Mil, the Initiating PI's existing military primary care-mental health services practice network, to access site health care leaders and potential study participants at the 6 study sites.

If effective, we expect that STEPS UP will increase the percentage of military personnel with unmet PTSD- and depression-related health care needs who get timely, effective, and efficient PTSD and depression care. Our real-world primary care effectiveness emphasis will prevent the Institute of Medicine's so called "15 year science to service gap." If successful, STEPS UP could roll out immediately, reinforcing and facilitating pathways to PTSD and depression recovery.

BODY:

The WRNMMC, RAND, RTI, University of Washington, Boston VA Research Institute (BVARI), USUHS, and HRPO IRBs have all approved the master protocol, consent form, and related study materials. During the past year, the study team received final IRB approval and began recruiting participants at the sixth study site, Ft. Bragg (February 2013). The study team also continued recruiting participants at the other five study sites: Joint Base Lewis-McChord (JBLM, Ft. Bliss, Ft. Campbell, Ft. Carson, and Ft. Stewart. As of August 31, 2013, 1,320 total referrals across all six sites had been received (427 referrals at JBLM, 283 at Ft. Bliss, 423 at Ft. Campbell, 53 at Ft. Carson, 82 at Ft. Stewart, and 52 at Ft. Bragg). A total of 666 participants had been enrolled and randomized into the study: 332 were enrolled and randomized into the STEPS UP arm of the study (124 at JBLM, 63 at Ft. Bliss, 100 at Ft. Campbell, 9 at Ft. Carson, 23 at Ft. Stewart, and 13 at Ft. Bragg), and 334 into the RESPECT-MIL arm (126 at JBLM, 63 at Ft. Bliss, 100 at Ft. Campbell, 9 at Ft. Carson, 23 at Ft. Stewart, and 13 at Ft. Bragg). Across all six recruitment sites, 419 potential participants were ineligible for various reasons, and 235 declined to participate.

We examined the existing baseline data to determine variability in our main outcome measures, and conducted a power analysis based on these data. Results of this analysis showed that we will have adequate power for the study to test the main outcomes with around 625 enrolled participants. We presented this work to the DSMB and they concurred that this plan appeared to be adequate. Dr. Jordan Irvin was informed of our plan to reduce the projected number of participants and stop enrollment as well. Recruitment stopped at five study sites at the end of June 2013 (JBLM, Ft. Bliss, Ft. Carson, Ft. Stewart, and Ft. Bragg), and recruitment stopped at Ft. Campbell at the end of July 2013.

Participants have reached eligibility for the 3-month follow-up assessment at all six of the study sites. As of August 31, 2013, 629 participants became eligible for the 3-month follow-up (245 at JBLM, 125 at Ft. Bliss, 170 at Ft. Campbell, 18 at Ft. Carson, 46 at Ft. Stewart, and 24 at Ft. Bragg); 556 participants have completed the 3-month follow-up assessment (217 at JBLM, 102 at Ft. Bliss, 158 at Ft. Campbell, 17 at Ft. Carson, 46 at Ft. Stewart, and 16 at Ft. Bragg), for an overall 3-month follow-up completion rate of 88%. We have also had a total of 493 participants reach eligibility for the 6-month follow-up (206 at JBLM, 108 at Ft. Bliss, 114 at Ft. Campbell, 16 at Ft. Carson, 40 at Ft. Stewart, and 9 at Ft. Bragg); 418 participants have completed the 6-month follow-up assessment (176 at JBLM, 81 at Ft. Bliss, 104 at Ft. Campbell, 12 at Ft. Carson, 37 at Ft. Stewart, and 8 at Ft. Bragg), for an overall 6-month follow-up completion rate of 85%. A total of 239 participants became eligible for the 12-month follow-up at five of the six recruitment sites (125 at JBLM, 52 at Ft. Bliss, 50 at Ft. Campbell, 2 at Ft. Carson, and 10 at Ft. Stewart); 181 participants have completed the 12-month follow-up assessment (97 at JBLM, 33 at Ft. Bliss, 41 at Ft. Campbell, 1 at Ft. Carson, and 9 at Ft. Stewart), for an overall 12-month follow-up completion rate of 76%.

Multiple amendments have been submitted to and approved by the WRNMMC IRB during the last year. In September 2012, the WRNMMC IRB approved an amendment allowing for reimbursement for off-duty participation in the trial to offset any burden that may result from participation in the study. In December 2012, the WRNMMC IRB approved an amendment that provided telephone interview and paper/pencil versions of the follow-up assessments, increased the number of qualitative study interview participants, revised SAE reporting language in the master protocol, and updated site and centralized personnel. The WRNMMC IRB also approved an amendment in December 2012 to allow investigators to manually check the study web portal automated eligibility determinations to ensure potential participants are correctly classified as eligible or ineligible for study participation. In March 2013, the WRNMMC IRB approved an amendment to cease the manual checks of the study web portal automated eligibility determinations, and continue a weekly automated check of all eligibility determinations. In May 2013, the WRNMMC IRB approved an amendment that made changes to the qualitative study, including shortening and simplifying the primary care provider qualitative interview and conducting the chart-assisted recall portion of the qualitative interviews with the nurse care facilitators rather than the primary care providers. In June 2013, the WRNMMC IRB approved an amendment modifying the study recruitment pamphlet to reflect the electronic Amazon.com gift cards that participants may be eligible to receive for their participation in the study. In July 2013, investigators submitted an amendment to the WRNMMC IRB to allow RTI to conduct batch tracing for lost-to-contact participants in order to get updated contact information to obtain follow-up data. In August 2013 we also submitted an amendment to the WRNMMC IRB to

digitize consent forms and store them centrally at RTI for the required 6 year time period rather than storing the hard copies at their respective posts. Both the batch tracing and consent form storage amendments are pending review with the WRNMMC IRB at this time.

The WRNMMC IRB has also approved several site-specific amendments during the past year. In September 2012, the WRNMMC IRB approved an amendment adding a new Site PI and RTI-hired full-time site coordinator at Ft. Carson, an amendment which updates Site PI contact information at Ft. Campbell, and an amendment adding a new RTI-hired full-time site coordinator at Ft. Stewart. In October 2012, the WRNMMC IRB approved an amendment adding a new RTI-hired half-time site coordinator at JBLM. In November 2012, the WRNMMC IRB approved an amendment adding a new Site PI and RTI-hired full-time site coordinator at Ft. Bragg. In March 2013, the WRNMMC IRB approved an amendment adding an interim Medical Monitor at Ft. Bliss, an amendment adding a new Medical Monitor at JBLM, and an amendment adding a new Site PI at Ft. Bragg. In April 2013, the WRNMMC IRB approved an amendment adding a new Site PI at Ft. Campbell. In May 2013, the WRNMMC IRB approved an amendment to increase the number of allowed enrollees from the JBLM site from 250 participants to 350 participants. In June 2013, the WRNMMC IRB approved an amendment to re-instate the previous Medical Monitor at Ft. Bliss, who had been on maternity leave and had returned to duty. In August 2013 the WRNMMC IRB approved an amendment adding a new Medical Monitor at JBLM.

On September 25, 2013, the RAND IRB approved the study in continuing review, and this renewal will be submitted to HRPO as soon as the paperwork is received. In November 2012, the WRNMMC IRB approved continuing review packages for the lead WRNMMC and six study site protocols for six months; the new expiration date for the lead WRNMMC and six study sites was May 7, 2013. The USUHS IRB issued secondary concurrence of the continuing review packages, and HRPO approved the continuing review packages in December 2012. The RTI IRB approved the study in continuing review in March 2013 and HRPO accepted this renewal in May 2013. In April 2013, the WRNMMC IRB approved continuing review packages for the lead WRNMMC and six study site protocols, which have a new expiration date set for May 7, 2014. The USUHS IRB issued secondary concurrence of the continuing review packages in May 2013, and HRPO approved the packages in June 2013. The University of Washington IRB approved the study in continuing review in July 2013 as well.

The STEPS-UP intervention has been developed and refined to include (1) a web-based care management support tool, called FIRST-STEPS; (2) a nurse-assisted web-based cognitive behavioral self management option, called DESTRESS-PC for PTSD; (3) a modularized telephonic cognitive-behavioral therapy option for PTSD and depression, called DESTRESS-T; and (4) a preference-based stepped care approach to primary care PTSD and depression treatment sequencing. A contract has been approved and signed by the Henry M. Jackson Foundation and Ultrasis, the developer of 'Beating the Blues,' a web-based therapy for depression that will be used in the STEPS UP trial; we have trained all seven care managers (six site care managers, one centralized care manager) to use Beating the Blues. Additional preparation in the past year has refined our recruitment strategy, finalized measures, refined final study methods, developed data collection procedures and forms, produced key materials (manuals, training materials, forms), and clarified safety procedures including inclusion criteria,

consent procedures, and confidentiality protections. Agreements addressing data use and sharing and publication are nearing completion.

Study investigators continued to participate in multiple routine weekly conference calls and other communications as necessary to ensure timely completion of all tasks. At the request of Dr. Jordan Irvin (CDMRP Science Officer), we have developed and submitted detailed timelines for regulatory approval and recruitment projections; we continue to update those documents to reflect current projections. In June 2013 we also submitted updated SOW's that are under review.

RTI has designed and launched the study web portal, including secure web-based study instrumentation, materials for site coordinators, and other study tools; we continue ongoing routine maintenance and evaluation of this site, as well as refinement of plans for the recruitment and follow-up process at each study location. We have also trained site coordinators at each study site regarding interaction with prospective participants, logistics for working with local care providers, and other process-oriented items, and RTI has continued to recruit, hire, and train site coordinators as necessary. During the past year, RTI has submitted a number of amendments to its internal IRB.

In the past year, RAND has refined the qualitative interview protocols and emergency procedures for the qualitative portion of the study and continued to conduct qualitative interviews. RTI is sharing identifying information on patients enrolled in the study with RAND, as permitted in the consent forms, and RAND is contacting those individuals to recruit them to participate in the interviews. RAND is filling cells as designated in the SOW to interview individuals early in the project, middle of the project, and late in the project, in both the STEPS UP and RESPECT-Mil conditions. Once recruited, each individual is interviewed 3 times during the course of their participation in the study. To date, RAND has recruited a total of 33 patients for the qualitative study and completed a total of 63 interviews with them (to date 9 of the 33 patients have completed all three interviews). Additional follow up interviews are pending. In addition, RAND completed early phase qualitative interviews with all eight nurse care facilitators and 1 late phase chart-assisted recall nurse care facilitator interview; the other seven are pending. RAND also completed 14 of the 30 planned semi structured interviews with health care providers across the six study sites; additional provider recruitment continues. RAND investigators continue to be involved in planning meetings, site visits, and conference calls.

BVARI investigators have continued to participate in weekly conference calls to discuss the overall study design, treatment development (e.g., web-based self-management intervention, phone-based therapy), recruitment strategies, and to provide supervision and oversight of the telehealth approaches to care. BVARI collaborators have modified DESTRESS-PC for STEPS UP trial use and developed the phone therapy (called DESTRESS-T) for trial use to include training materials, manuals, and treatment workbooks. The telephone therapy and related materials have been modified for trial use; the therapy is a broad-based ideographic modularized approach to telephone therapy that entails ten therapeutic modules that are disseminated to patients and therapists with the purpose of being used in conjunction with phone-based therapy. BVARI collaborators continue to provide supervision and training to the two half-time centralized psychologists who deliver the telephone therapy, as well as to the STEPS UP care

managers who have been trained to manage DESTRESS-PC. Additionally, we have continued training for behavioral activation and motivational interviewing with the care managers. During the past year, BVARI collaborators began to be available as needed for telephonic consultation with the STEPS UP care managers, to provide additional clinical assistance for difficult cases and one-on-one training in clinical strategies. BVARI collaborators also began to participate in the weekly individual staffing calls with each STEPS UP care manager in order to help track study patients being staffed and record staffing notes.

During the past year, University of Washington collaborators have continued to refine and develop training for the STEPS UP trial intervention and have developed working drafts of the care management manual. They have also continued more intensive supervision related to care management practices across all study sites. University of Washington investigators attend weekly telephone conferences to contribute to care manager coaching, therapy development, FIRST-STEPS enhancements, and general study implementation; they also continue to attend the University of Washington STEPS UP internal team meeting that is held approximately once each quarter.

In September 2012, the STEPS UP team conducted a “kick-off” site visit to Ft. Carson. In January 2013, the team conducted a series of site visits to all six study sites in order to discuss study progress with site personnel and local providers. In May 2013 we hired and trained a new STEPS UP study care manager at the Ft. Stewart site.

During the past year, the STEPS UP team held two meetings with the DSMB. The first meeting of the DSMB was held in November 2012, where Dr. John Freedy was elected as DSMB Chair, and the second meeting was held in April 2013. We continue correspondence with the DSMB as needed, and plan to hold the next DSMB meeting in January 2014.

As is the case in all clinical trials and longitudinal studies, recruitment and retention are a full time concern. The predominantly young, male and highly mobile military demographic profile is a key issue. Our experience accomplishing controlled trials in this population has been an asset, and we have aggressively sought innovative recruitment and retention strategies. During this past year, we began distributing reimbursement for study participation in the form of Amazon.com gift cards. We also began holding monthly calls with all of the study Site PI’s, as well as regular calls every other week with all of the STEPS UP and regular RESPECT-Mil care facilitators at the six study sites. The purpose of these calls was to discuss any potential barriers to recruitment and retention of participants in the study, and brainstorm solutions to address these barriers. These regular calls were also useful so investigators can better understand local issues occurring at the sites that may have an impact on study participation. We have ceased the regular calls every other week with all of the STEPS UP and regular RESPECT-Mil care facilitators since ending recruitment at the sites, but plan to continue holding regular calls with the Site PI’s.

In October 2012, we uncovered programming issues with the survey that resulted in some misclassification of cases within the project. During the quarter from December 2012 to February 2013, we consulted with the IRBs and DSMB over specific plans for informing participants and for data analysis. The DSMB, RAND, RTI and WRNMMC IRBs have

concurrent with our proposed plan. At this time, we believe the issues are fully resolved, but continue to implement checking procedures to ensure there are not any additional errors. In March 2013, the WRNMMC IRB approved an amendment to cease the manual checks of the study web portal automated eligibility determinations, and continue a weekly automated check of all eligibility determinations. To date, 706 soldiers have been screened for study eligibility from October 10, 2012 – August 23, 2013 and no errors were found based on our eligibility checks.

Customization of the FIRST-STEPS web-based care management software for the STEPS UP trial is ongoing but for practical purposes FIRST-STEPS is up and running; ongoing modifications will not threaten the fidelity of intervention or the validity of trial results.

During the next quarter, we plan to continue follow-up at all six study sites and begin preliminary data analysis on the baseline data. We will also continue to ensure compliance with all IRB administrative requirements and meet with IRB chiefs and HRPO representatives to coordinate an efficient process for ongoing regulatory submission and approval. We will continue with ongoing care manager training and coaching at each site with weekly individual staffing and group coaching calls, and will conduct site visits at any data collection sites as necessary. In addition, we will begin work on a study design paper during the next quarter.

The Initiating Principal Investigator (PI), COL Charles Engel, will be retiring from the military during the next quarter. Due to the change in status from military to contractor, he was advised to transition from PI to Associate Investigator (AI). Dr. Engel will remain involved in study-related activities. We are preparing for a PI change that will move Dr. Michael Freed from AI to PI.

KEY RESEARCH ACCOMPLISHMENTS:

There are not yet any clear scientific findings resulting from this research as we are still in the data collection phase. Results are expected in June 2015.

REPORTABLE OUTCOMES:

The following presentation has been accepted for the Annual International Society for Traumatic Stress Studies (ISTSS) Meeting in November 2013 in Philadelphia, PA:

Engel CC, Freed MC, Lane B, Jaycox L, Bray R, Zatzick D, Litz B. (November 2013) DoD STEPS-UP: Design, Roll-Out and Early Lessons from a Randomized Effectiveness Trial of Collaborative PTSD Care in Army Primary Care. Part of ISTSS Symposium: Interventions for PTSD in Primary Care Medical Settings: Implementation and Early Effectiveness Outcomes. Meredith L (chair) & Zatzick D (discussant). International Society for Traumatic Stress Studies (ISTSS) conference, Philadelphia, PA.

CONCLUSION:

There are no conclusions to report at this time, as the study is still in the data collection phase.

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Litz, B. T., Engel, C. C., Bryant, R., & Papa, A. (2007). A Randomized, Controlled Proof-of-Concept Trial of an Internet-Based, Therapist-Assisted Self-Management Treatment for Posttraumatic Stress Disorder. *American Journal of Psychiatry*, 164(11), 1676-1683.

APPENDICES:

N/A

SUPPORTING DATA:

N/A